

Exploring Systems Biology Approaches to Traditional Chinese Medicine Cancer Research

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Abstract— Cancer is a chronic, complex disease. With advanced high-throughput technologies i.e. various -omics approaches, molecular imaging and computer technologies, conventional medicine and its research of cancer is leading to the emergence of systems biology. Traditional Chinese Medicine (TCM) focuses on the diseased person as a whole to formulate the therapeutic strategies to create a holistic systemic approach to treat the imbalanced systems of a person. TCM practices are usually descriptive, and empirical. To facilitate cross discipline dialog, and potentially research collaboration, it is important to move TCM research toward systems biological approaches. Analysis of FY2006 and 2007 NCI funded TCM research grants portfolio and research approaches will be discussed.

Keywords—component; cancer; sytems biology; Traditional Chinese Medicine.

1. INTRODUCTION

The realization that cancer is a chronic complex disease developed from a variety of molecular alterations within intracellular pathways [1], along with advances in high-throughput technologies (-omics), molecular imaging, computer

technologies, is leading a departure from the "reductionist approach" and the emergence of systems biology approaches to conventional biomedical practice and research [2]. Systems biology is an integrative approach to scientific research which involves experimental biology, computer sciences, engineering, mathematics, physics, and other disciplines to understand the complex and dynamic interactions of biological systems, from single cells, tissues, and organs to complete organisms and possibly to whole ecosystems. Traditional Chinese Medicine (TCM) is a holistic approach to care, which focuses on the person as a whole, recognizing the importance of the dynamic interconnectedness of organs and between the person and his environment. From this perspective therapeutic strategies are formulated to treat the imbalanced systems of a person.

Here we seek to explore a rationale for exploring possible convergences between Traditional Chinese Medicine (TCM), and the systems biology/systems medicine paradigm.

2. ANALYSIS OF NCI FUNDED TCM RESEARCH GRANTS AND RESEARCH APPROACHES

We conducted analyses of NCI's complementary and alternative medicine (CAM) portfolio for Fiscal Year (FY) 2004 through FY 2008. Figure 1 shows that estimated National Cancer Institute (NCI) CAM research expenditures exceeded \$121 million in each FY

from 2004 through 2008. At NCI, CAM interventions are sorted into the following eight categories: Alternative Medical Systems, Energy Therapies, Exercise Therapies, Manipulative and Body-based Methods, Mind-body Interventions, Nutritional Therapeutics, Pharmacological and Biologic Treatments, and Spiritual Therapies. TCM is included within the Alternative Medical Systems category and research into aspects of TCM represents almost all of NCI's expenditures in that category. An analysis of the TCM components of NCI's portfolio shows that in FY 2006 and 2007, thirty nine research grants were funded. Thirty five of these grants evaluated natural products from the pharmacopeia of TCM; six grants examined acupuncture and one qigong as shown in Figure 2. Some of these grants have more than one type of TCM interventions. The TCM research projects were mainly focused on cancer treatment and prevention. Nineteen grants had projects on cancer treatment, and fourteen on cancer prevention. Acupuncture and qigong projects were focused on symptoms/side-effect managements, while the majority of natural products projects studied treatment or prevention.

We next analyzed the research approaches or research design of these projects. Five acupuncture grants were clinical trials, and one was an epidemiology study. Even though the TCM theory for acupuncture application reflects a type of "systems medicine" thinking, none of these grants used systems biology approaches (e.g. – omics technologies). Among natural products projects, five grants were clinic trials. Twenty eight grants were preclinical in vitro and in vivo research. Two were epidemiology studies. Only two out of thirty five natural products research grants used microarray or high through put technology. One project used gene expression microarray, and another used protein antibody microarray.

Twenty three of the grants conducted research with a single active agent from a plant or fungi for the purpose of drug discovery. Eight of the grants used multi-fractions, or extracts of a single natural product. Two of the studies used multi-herbs or herbal formula. The preclinical in vitro cell

studies were mainly focused on the molecular and cellular pathways of a particular cancer cell type. Animal studies were also mainly focused on a cancer tissue.

Only two of these thirty nine TCM projects used high through put –omics technology in their research design and approaches suggests that there is a lack of incorporate this technology application in TCM research. None of the projects used a computational modeling approach. This could possibly be partly due to the scientific research training background of TCM cancer researcher. It could also partly be due to the grant funding issues, e.g. more than 50% of these projects were supported by R21 grants which are designed to support developmental research.

3. SYSTEMS BIOLOGY FUNDING OPPORTUNITIES

We also conducted an analysis of NIH Funding Opportunities for systems biology. NIH has recognized the importance of the systems biology approach for biomedical research. Since 2003, at least 48 RFAs, PAs and PARs have considered the systems biology approach as one of the research objectives. Ten announcements mainly focused on systems biology. NCI released RFA-CA-04-013 on 12/01/2003, titled: INTEGRATIVE CANCER BIOLOGY PROGRAMS. From that RFA, nine integrative biology centers were funded. NICHD, NIDCR, NIGMS, and NHLBI also released announcements soliciting applications in the field of systems biology since 2004. The list of some NIH systems biology related FOAs from 2003-2007 is in Figure 3.

4. CONCLUSION

TCM diagnosis and treatment theory is based on a dynamic whole person systems approach. Cancer researchers should consider the use of systems biology approaches to better understand the effects of TCM interventions. Our analysis indicates that this is only done occasionally in NCI supported TCM research. With the progress of modern science and technology, opportunities are

emerging to explore the applicability of systems biology thinking to TCM research and practice. Such an exploration may bring a greater scientific rigor to these emerging fields. Using high-throughput technologies (-omics), molecular imaging, computer technologies and developing experimental and computational model systems with the systems approaches to cancer and TCM cancer research could improve our understanding of effective ways to treat cancer and foster a better cancer care.

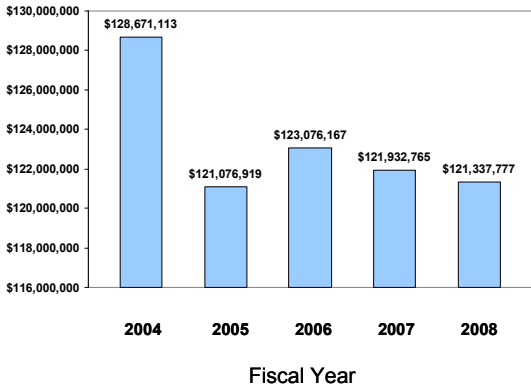


Figure 1. NCI FY04-08 CAM Expenditures: *includes grants, cooperative agreements, intramural projects, and contracts which NCI is the primary funding IC and excludes training grants (T, F, K, R25s)*

5. REFERENCE

[1] D. hanahan and R. A Weinberg “The hallmarks of Cancer”, Cell, Jan 2000, 100 (1), pp. 57-70

[2] L. Hood, J. R. Heath, M. E Phelps and B. Lin “Systems biology and new technologies enable predictive and preventative medicine.”, Science, Oct 2000, 306(5696):640-3.

	Total Number of Grants	Symptom/Side-effect Management	Prevention	Treatment	Epidemiology
Total TCM Grants	39	7	14	19	2
Natural Products	35	2	14	19	2
Acupuncture	6	5	0	0	1
Qigong	1	1	0	0	0

Figure 2. NCI FY06-07 Funded TCM Research Grants

Announcement Number	Issuing Organization	Release Date	Expiration Date	Activity Code(s)	Title
RFA-CA-04-013	NCI	12/1/2003	4/14/2004	P20, P50	INTEGRATIVE CANCER BIOLOGY PROGRAMS
RFA-HL-06-004	NHLBI	11/18/2005	3/11/2006	R33	NHLBI Exploratory Program in Systems Biology (R33)
RFA-HL-07-005	NHLBI	6/5/2006	9/26/2007	R33	NHLBI Exploratory Program in Systems Biology (R33)
PAR-08-054	NICHD	12/18/2007	5/26/2010	T32	Ruth L. Kirschstein National Research Service Award (NRSA) Institutional Predoctoral Training Program in Systems Biology of Developmental Biology & Birth Defects(T32)
RFA-DE-08-001	NIDCR	3/16/2007	11/15/2007	R01	A Systems Approach to Salivary Gland Biology (R01)
RFA-DE-08-002	NIDCR	3/16/2007	11/16/2007	K25	NIDCR Mentored Quantitative Research Development Award in A Systems Approach to Salivary Gland Biology (K25)
RFA-GM-05-010	NIGMS	9/22/2004	2/26/2005	P50	NIGMS National Centers for Systems Biology
RFA-GM-07-004	NIGMS	7/7/2006	11/22/2006	P50	NIGMS National Centers for Systems Biology (P50)
RFA-GM-08-004	NIGMS	6/11/2007	10/23/2007	P50	NIGMS National Centers for Systems Biology (P50)
RFA-GM-08-001	NIGMS	4/24/2007	10/24/2007	R01	Collaborative Studies on Systems Biology of Complex Phenotypes (R01)

Figure 3. NIH Systems Biology FOAs from 2003-2007